

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a fusion polypeptide comprising a reporter protein and at least two
5 different heterologous protein destabilization sequences, which fusion polypeptide has a reduced half-life relative to a corresponding reporter protein which lacks the heterologous protein destabilization sequences or has a reduced half-life relative to a corresponding reporter protein which has one of the heterologous protein destabilization sequences.
10
2. An isolated nucleic acid molecule comprising a nucleic acid sequence comprising an open reading frame for a reporter protein and at least two heterologous destabilization sequences, wherein one of the heterologous destabilization sequences is a mRNA destabilization sequence and another is a
15 heterologous protein destabilization sequence.
3. An isolated nucleic acid molecule comprising a nucleic acid sequence comprising an open reading frame for a luciferase and at least one heterologous destabilization sequence, wherein a majority of codons in the open reading frame
20 for the luciferase are codons which are preferentially employed in a selected host cell.
4. The isolated nucleic acid molecule of claim 1, 2 or 3 further comprising a promoter operably linked to the nucleic acid sequence.
25
5. The isolated nucleic acid molecule of claim 4 wherein the promoter is a regulatable promoter.
6. The isolated nucleic acid molecule of claim 5 wherein the promoter is an
30 inducible promoter.

7. The isolated nucleic acid molecule of claim 5 wherein the promoter is a repressible promoter.
8. The isolated nucleic acid molecule of claim 1 further comprising a
5 heterologous mRNA destabilization sequence.
9. The isolated nucleic acid molecule of claim 2 or 8 wherein the mRNA destabilization is 3' to the nucleic acid sequence.
- 10 10. The isolated nucleic acid molecule of claim 1 or 2 wherein the nucleic acid sequence encoding at least the reporter protein is optimized for expression in a host cell.
11. The isolated nucleic acid molecule of claim 1 or 2 wherein the reporter
15 protein encodes a luciferase.
12. The isolated nucleic acid molecule of claim 1 wherein the reporter protein encodes a beetle luciferase.
- 20 13. The isolated nucleic acid molecule of claim 12 wherein the reporter protein encodes a click beetle luciferase.
14. The isolated nucleic acid molecule of claim 1 wherein the reporter protein encodes an anthozoan luciferase protein.
- 25 15. The isolated nucleic acid molecule of claim 3 wherein the heterologous destabilization sequence is a protein destabilization sequence.
16. The isolated nucleic acid molecule of claim 3 wherein the heterologous
30 destabilization sequence is a mRNA destabilization sequence.

17. The isolated nucleic acid molecule of claim 1, 2 or 3 wherein nucleic acid sequence comprises SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:66, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, or a fragment thereof that encodes a fusion polypeptide with substantially the same activity as the corresponding full-length fusion polypeptide encoded by SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:66, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79 or SEQ ID NO:80.

18. The isolated nucleic acid molecule of claim 1 further comprising a mRNA destabilization sequence.

19. The isolated molecule of claim 18 wherein one protein destabilization sequence is a PEST sequence.

20. The isolated nucleic acid molecule of claim 1 or 2 wherein one heterologous protein destabilization sequence is a PEST sequence.

20

21. The isolated nucleic acid molecule of claim 1 or 2 wherein one heterologous protein destabilization sequence is from the C-terminus of a mammalian ornithine decarboxylase.

22. The isolated nucleic acid molecule of claim 1 or 2 wherein one heterologous protein destabilization sequence is a mutant ornithine decarboxylase sequence.

23. The isolated nucleic acid molecule of claim 21 wherein the mutant ornithine decarboxylase sequence has an amino acid substitution at a position corresponding to position 426, 427, 428, 430, 431, 433, 434, 439 or 448 of murine ornithine decarboxylase.

30

24. The isolated nucleic acid molecule of claim 1 or 2 wherein one heterologous protein destabilization sequence is CL1, CL2, CL6, CL9, CL10, CL11, CL12, CL15, CL16, CL17 or SL17.
- 5
25. The isolated nucleic acid molecule of claim 1 or 2 wherein one heterologous protein destabilization sequence is at the C-terminus of the reporter protein.
26. The isolated nucleic acid molecule of claim 1 or 2 wherein one heterologous protein destabilization sequence at the N-terminus of the reporter protein.
- 10
27. The isolated nucleic acid molecule of claim 1 or 2 further comprising an ubiquitin polypeptide at the N-terminus of the fusion polypeptide.
- 15
28. The isolated nucleic acid molecule of claim 27 wherein one of the heterologous protein destabilization sequences is at the C-terminus of ubiquitin.
29. The isolated nucleic acid molecule of claim 28 wherein one of the heterologous protein destabilization sequences comprises a glutamic acid or arginine residue.
- 20
30. The isolated nucleic acid molecule of claim 10 which encodes a fusion polypeptide with a half-life of expression of about 20 minutes.
- 25
31. The isolated nucleic acid molecule of claim 10 which encodes a fusion polypeptide with a half-life of expression of about 30 minutes.
32. The isolated nucleic acid molecule of claim 15 wherein the heterologous protein destabilization sequence is a PEST sequence.
- 30

33. The isolated nucleic acid molecule of claim 15 wherein the heterologous protein destabilization sequence is from the C-terminus of a mammalian ornithine decarboxylase.
- 5 34. The isolated nucleic acid molecule of claim 15 wherein the heterologous protein destabilization sequence is CL1, CL2, CL6, CL9, CL10, CL11, CL12, CL15, CL16, CL17 or SL17.
35. A vector comprising the nucleic acid molecule of claim 1, 2 or 3.
- 10 36. The vector of claim 35 wherein the nucleic acid molecule is operably linked to a regulatable promoter.
37. The vector of claim 36 wherein the promoter is a repressible promoter.
- 15 38. The vector of claim 34 wherein the nucleic acid molecule comprises SEQ ID NO:49, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80 or a fragment thereof that encodes a fusion polypeptide with substantially the same activity as the corresponding full-length fusion polypeptide encoded by SEQ ID NO:49, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79 or SEQ ID NO:80.
- 20 39. A fusion polypeptide encoded by the nucleic acid molecule of claim 1, 2 or 3.
- 25 40. The fusion polypeptide of claim 38 wherein the reporter protein is chloramphenicol acetyltransferase, luciferase, beta-glucuronidase or beta-galactosidase.
- 30 41. A host cell comprising the vector of claim 35.

42. The host cell of claim 41 which is stably transfected with the vector that encodes a fusion polypeptide comprising a luminescent protein.
43. The host cell of claim 42 wherein the signal emitted by the host cell comprising the vector is greater than the signal emitted by a corresponding host cell comprising a vector which lacks one or more of the destabilization sequences.
44. A stable cell line comprising the vector of claim 35 wherein the signal emitted by the reporter protein is equal to or greater than a signal emitted by a corresponding stable cell line comprising a vector which lacks one or more of the heterologous destabilization sequences.
45. A method to detect a reporter protein in a cell, comprising:
a) contacting a cell with the vector of claim 35; and
b) detecting or determining the presence or amount of the reporter protein in the cell or a lysate thereof.